OMB INFORMATION COLLECTION
SUPPORTING STATEMENT
0910-0308

Adverse Experience Reporting for Licensed Biological Products; and General Records

JUSTIFICATION

1. Circumstances Making This Information Collection Necessary

The Food and Drug Administration (FDA) is requesting an extension of Office of Management and Budget (OMB) Control No. 0910-0308 and OMB approval of the information collection requirements in 21 CFR Part 600 listed below:

21 CFR 600.80(c)(1)	Reporting	Requires licensed manufacturers to report each adverse experience that is both serious and unexpected, whether foreign or domestic, as soon as possible but in no case later than 15 calendar days of initial receipt of the information by the licensed manufacturer. Also requires licensed manufacturers to submit any follow-up reports within 15 calendar days of receipt of new information or as requested by FDA.
21 CFR 600.80(c)(2)	Reporting	Requires licensed manufacturers to report each adverse experience not reported in a postmarketing 15-day Alert report (21 CFR 600.80 (c) (1) (i)) at quarterly intervals, for 3 years from the date of issuance of the product license, and then at annual intervals.
21 CFR 600.80(e)	Reporting	Requires licensed manufacturers to submit a 15-day Alert report for an adverse experience obtained from a postmarketing clinical study only if there is a reasonable possibility that the product caused the adverse experience.
21 CFR 600.81	Reporting	Requires licensed manufacturers to submit, at an interval of every 6 months, information about the quantity of the product distributed under the biologics license, including the quantity distributed to distributors.
21 CFR 600.90	Reporting	Licensed manufacturers may submit a waiver request for any requirement that applies to the licensed manufacturer under 21 CFR 600.80 and 600.81. A waiver request must include supporting documentation.

21 CFR 600.12(a), (c), (d) & (e)	Recordkeeping	Requires, among other things, concurrently with the performance of each step that all records of each step in the manufacture and distribution of a product be made and retained for no less that 5 years after the records of manufacture have been completed or 6 months after the latest expiration date for the individual products, whichever represents a later date.
21 CFR 600.12(b)(2)	Recordkeeping	Requires manufacturers to maintain complete records pertaining to the recall from distribution of any product.
21 CFR 600.80(i)	Recordkeeping	Requires licensed manufacturers to maintain for a period of 10 years records of all adverse experiences known to the licensed manufacturer, including raw data and any correspondence relating to the adverse experiences.

Under the Public Health Service Act (42 U.S.C. 262), FDA is required to ensure the marketing of only those biological products, that are safe and effective. FDA must, therefore, be promptly informed of all adverse experiences occasioned by the use of licensed biological products. FDA issued the adverse experience reporting (AER) requirements in 21 CFR Part 600 to enable FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to licensed biological products. The primary purpose of FDA's AER system is to flag potentially serious safety problems with licensed biological products, focusing especially on newly licensed products. Although premarket testing discloses a general safety profile of a biological product's comparatively common adverse effects, the larger and more diverse patient populations exposed to the licensed biological product provides the opportunity to collect information on rare, latent, and long-term effects. Reports are obtained from a variety of sources, including patients, physicians, foreign regulatory agencies, and clinical investigators. Information derived from the AER system contributes directly to increased public health protection because such information enables FDA to recommend important changes to the product's labeling (such as adding a new warning), to initiate removal of a biological product from the market when necessary, and to assure the manufacturer has taken adequate corrective action, if necessary.

Licensed manufacturers are required to report to FDA on all serious and unexpected adverse reactions regardless of the source from which the manufacturer obtained the reaction information. These reports are filed using the MEDWATCH Form FDA-3500A (approved under OMB No.0910-0291) or the Vaccine Adverse Experience Reporting System Form (VAERS-1). Section 321 of the National Childhood Vaccine Injury Act (NCVIA, Public Law 99-660) specifically addresses the waiver of paperwork reduction in the implementation of this statute. Under § 600.80 (f)(3), a manufacturer may also use an alternative report form provided the format is equivalent to all elements of information specified in the designated forms and the format is pre-approved by MEDWATCH or FDA.

The general recordkeeping provisions under § 600.12 require manufacturers to maintain records of each step in the manufacture and distribution of products. These requirements provide FDA with the necessary information to help ensure the safety, purity, and potency of biological products.

2. Purpose and Use of the Information

The primary purpose of FDA's AER system is to flag potentially serious safety problems with licensed biological products, focusing especially on newly licensed products. Although premarket testing discloses a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the licensed biological product provides, for the first time, the opportunity to collect information on rare, latent, and long-term effects. Reports are obtained from a variety of sources, including patients, physicians, foreign regulatory agencies, and clinical investigators. Information derived from the adverse experience reporting system contributes directly to increase public health protection because such information enables FDA to recommend important changes to the product's labeling (such as adding a new warning) and, when necessary, to initiate removal of a biological product from the market and to ensure that the manufacturer has taken adequate corrective action, if necessary. The semiannual distribution report allows FDA to see the quantity, the lot number, and the dosage of different products. This allows FDA to estimate more accurately the incidence of a product's adverse effects in relation to the volume of the product distributed.

The recordkeeping requirements serve preventative and remedial purposes by establishing accountability and traceability in the manufacture and distribution of products. These requirements enable FDA to perform meaningful inspections. Without this information, FDA could not monitor industry procedures and discharge its statutory responsibility for protecting the nation's health.

3. Use of Improved Information Technology and Burden

Most of the information required under the AER regulations is submitted using FDA Form 3500A or VAERS-1. Both versions of the forms and instructions are available on the Internet. The forms can be downloaded so that computers can be used to fill out and print the report, which can then be mailed or faxed to the agency.

Licensed manufacturers may use computers, discs, tapes, microfiche or microfilm in lieu of hard copy records for the purpose of maintaining records. Computers may be used for filing distribution records. FDA is not aware of any other improved technology to reduce the burden.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only agency that requires this information. The required information is not available from any other source.

5. Impact on Small Businesses or Other Small Entities

FDA believes that the regulations should apply equally to all enterprises. While FDA does not believe it can apply different standards with respect to statutory requirements, FDA does provide special help to small businesses. The Center for Biologics Evaluation and Research (CBER), Office of Communication, Training, and Manufacturers Assistance, provides assistance to small businesses concerning FDA's regulatory requirements. The Center for Drugs Evaluation and Research (CDER), Division of Drug Information also provides assistance to small businesses.

6. Consequences of Collecting Information Less Frequently

Less frequent data collection would delay identification of biological products believed responsible for adverse reactions, including permanent injuries and fatalities. Appropriate FDA action such as withdrawal from the market or changes in labeling would also be delayed.

There are no technical or legal obstacles to reducing the burden.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The licensed manufacturers are required to submit to FDA a 15-day Alert report for each serious and unexpected adverse experience. This requirement enables FDA to promptly investigate and, when necessary, initiate corrective action to protect the public from potential adverse product interactions.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), a 60-day notice for public comment on the information collection provisions was published in the **Federal Register** of February 15, 2008 (73 FR 8881). No comments were received from the public.

9. Explanation of Any Payment or Gifts to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

The confidentiality of information received by FDA is consistent with the Freedom of Information Act (FOIA) and the agency's regulations under 21 CFR Part 20, which prohibit FDA from releasing to the public the names of patients, individual reporters, health care practitioners, hospitals, and any geographical identifiers. Such information is deleted from any information released by FDA under FOIA and FDA regulations.

11. Justification for Sensitive Questions

Questions of a sensitive nature are not applicable to this information collection.

12. Estimates of Annualized Burden Hours and Costs

The estimated annual burden for this information collection is 895,639 hours.

Estimated Annual Reporting Burden					
21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.80(c)(1) & 600.80(e)	88	270.85	23,835	1	23,835
600.80(c)(2)	88	248.55	21,872	28	612,416
600.81	88	2.03	179	1	179
600.90	6	1	6	1	6
TOTAL					636,436

Respondents to this collection of information are manufacturers of biological products. The number of respondents is based on the estimated number of manufacturers that submitted the required information to the CBER and CDER, FDA, in fiscal year (FY) 2006. Based on information obtained from the FDA's database system, there were 88 licensed biologics manufacturers. This number excludes those manufacturers who produce blood and blood components and in-vitro diagnostic licensed products, because § 600.80(k) specifically exempts manufacturers of these products from adverse experience reporting requirements. The total annual responses are based on the estimated number of submissions received annually by FDA in FY 2006. However, not all manufacturers have submissions in a given year and some may have multiple submissions. There were an estimated 23,835 15-day Alert reports, 21,872 periodic reports, and 179 lot distribution reports submitted to FDA. The number of 15-day Alert reports for postmarketing studies under § 600.80(e) is included in the total number of 15-day Alert reports. FDA received 6 requests for waiver under § 600.90, all of which were granted. The hours per response are based on FDA experience. The burden hours required to complete the MedWatch Form for § 600.80(c)(1), (e), and (f) are reported under OMB Control No. 0910-0291.

Estimated Annual Recordkeeping Burden					
21 CFR Section	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record	Total Hours
600.12	112	47.24	5,291	32	169,312
600.12(b)(2)	303	6.08	1,842	24	44,208
600.80(i)	88	519.40	45,707	1	45,707
TOTAL					259,227

The number of respondents is based on the number of manufacturers subject to those regulations.

Based on information obtained from FDA's database system, there were 303 licensed manufacturers of biological products in FY 2006. However, the number of recordkeepers listed for § 600.12(a)-(e), excluding (b)(2), is estimated to be 112. This number excludes manufacturers of blood and blood components because their burden hours for recordkeeping have been reported under § 606.160 in OMB Control No. 0910-0116. The number of total annual records is based on the annual average of lots released (5,291), number of recalls made (1,841), and total number of adverse experience reports received (45,707) in FY 2006. The hours per record are based on FDA experience.

Cost to Respondents

The estimated annualized cost to the respondents is $40,893,905.

Cost to Respondents			
Activity	Number of Hours	Cost per Hour	Total Cost
Reporting	636,436	$50	$31,821,800
Recordkeeping	259,203	$35	$9,072,105
TOTAL			$40,893,905

This cost is based on an average pay rate of $50.00 per hour for an upper level manager, and mid-level professional that handle the various reporting requirements. This cost is also based on a pay rate of $35 per hour for a mid-level professional who has the training and skills to handle the various recordkeeping requirements. This salary estimate includes benefits but no overhead costs.

13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

There are no capital costs or operating and maintenance costs associated with this collection of information.

14. Annualized Cost to the Federal Government

The estimated annual cost to FDA is $12,500,958.

Annual Cost to FDA				
Activity	Number of Reports	Hours per Report	Cost per Hour	Total Cost
Report Distribution	636,436	0.1	$21	$1,336,516
Report Review	636,436	0.33	$52	$10,921,242
TOTAL				$12,257,758

This cost is based on a GS-7 Consumer Safety Technician who is responsible for distributing the report. This cost is also based on a GS-14 Reviewer who is responsible for reviewing the reports. The salaries include benefits but no overhead costs.

Annual Cost to FDA

Activity	Number of Respondents	Hours per Inspection	Cost per Hour	Total Cost
Inspection	152	40	$40	$243,200

There are 303 licensed manufacturers of biological products that will be inspected on a biennial basis. Therefore it is estimated that approximately one-half (152 establishments) will be inspected annually. The cost estimate is based on a FDA inspector at an average grade of GS-12/5 who takes an average of 40 hours for each establishment to perform the on-site inspection, review the records, and write the report.

15. Explanation for Program Changes or Adjustments

The estimated total annual burden for this information collection was 493,522 hours in 2005. The current increase to 895,639 burden hours is mostly attributed to the increase in the number of reports (total annual responses) submitted under 21 CFR 600.80.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no results to publish for this information collection.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA is not seeking approval to exempt display of the expiration date for OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

Not applicable.